10/ 775,699

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1202txn

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	SEP 09	ACD predicted properties enhanced in REGISTRY/ZREGISTRY
NEWS 4	OCT 03	MATHDI removed from STN
NEWS 5	OCT 04	CA/CAplus-Canadian Intellectual Property Office (CIPO) added to core patent offices
NEWS 6	OCT 13	New CAS Information Use Policies Effective October 17, 2005
NEWS 7	OCT 17	STN(R) AnaVist(TM), Version 1.01, allows the export/download of CAplus documents for use in third-party analysis and visualization tools
NEWS 8	OCT 27	Free KWIC format extended in full-text databases
NEWS 9	OCT 27	DIOGENES content streamlined
NEWS 10	OCT 27	EPFULL enhanced with additional content
NEWS 11	NOV 14	CA/CAplus - Expanded coverage of German academic research
NEWS 12	NOV 30	REGISTRY/ZREGISTRY on STN(R) enhanced with experimental spectral property data

NEWS EXPRESS NOVEMBER 18 CURRENT VERSION FOR WINDOWS IS V8.01,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005.
V8.0 USERS CAN OBTAIN THE UPGRADE TO V8.01 AT
http://download.cas.org/express/v8.0-Discover/

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 17:23:51 ON 30 NOV 2005

=> file reg
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION

10/ 775,699

FULL ESTIMATED COST 0.21 0.21

FILE 'REGISTRY' ENTERED AT 17:24:35 ON 30 NOV 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 29 NOV 2005 HIGHEST RN 868943-57-1
DICTIONARY FILE UPDATES: 29 NOV 2005 HIGHEST RN 868943-57-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

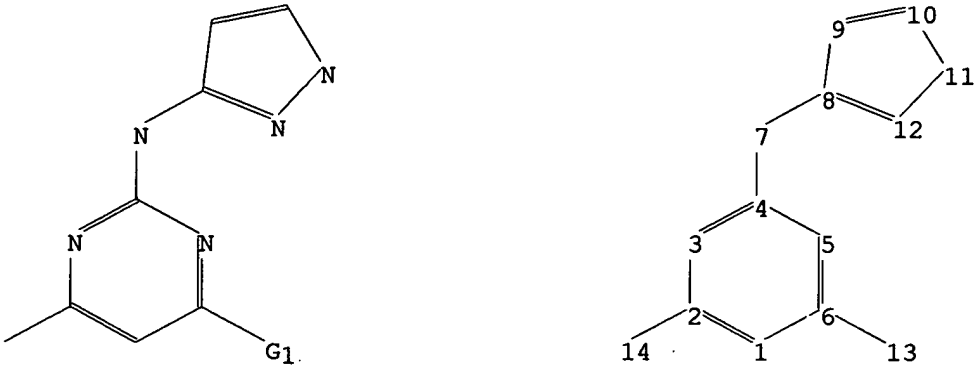
****
*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10775699.str



chain nodes :
7 13
ring nodes :
1 2 3 4 5 6 8 9 10 11 12
ring/chain nodes :

10/ 775,699

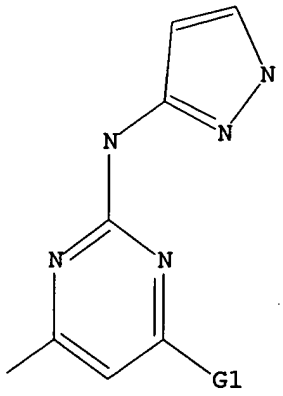
14
chain bonds :
4-7 6-13 7-8
ring/chain bonds :
2-14
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 8-9 8-12 9-10 10-11 11-12
exact/norm bonds :
2-14 4-7 6-13 7-8 8-9 8-12 9-10 10-11 11-12
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

G1:C,O,S,N

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:CLASS 14:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 C,O,S,N

Structure attributes must be viewed using STN Express query preparation.

=> s l1 sample
SAMPLE SEARCH INITIATED 17:25:04 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 60 TO ITERATE

100.0% PROCESSED 60 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 736 TO 1664
PROJECTED ANSWERS: 0 TO 0

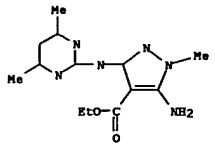
L2 0 SEA SSS SAM L1

```
=> s l1 full
FULL SEARCH INITIATED 17:25:10 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      1438 TO ITERATE

100.0% PROCESSED     1438 ITERATIONS                                 23 ANSWERS
SEARCH TIME: 00.00.01

L3            23 SEA SSS FUL L1

=> file hcaplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   161.33     161.54

FILE 'HCAPLUS' ENTERED AT 17:25:17 ON 30 NOV 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)
```



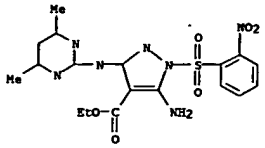
```
FILE COVERS 1907 - 30 Nov 2005  VOL 143 ISS 23
FILE LAST UPDATED: 29 Nov 2005  (20051129/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d his

     (FILE 'HOME' ENTERED AT 17:23:51 ON 30 NOV 2005)

     FILE 'REGISTRY' ENTERED AT 17:24:35 ON 30 NOV 2005
L1              STRUCTURE UPLOADED
L2            0 S L1 SAMPLE
L3           23 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 17:25:17 ON 30 NOV 2005

=> s l3
L4            9 L3

=> d l4 1- ibib abs hitstr
YOU HAVE REQUESTED DATA FROM 9 ANSWERS - CONTINUE? Y/(N):y
```

L4 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:387769 HCAPLUS
DOCUMENT NUMBER: 143:357022
TITLE: Ethyl 5-amino-3-(4,6-dimethylpyrimidin-2-ylamino)-1-methyl-1H-pyrazole-4-carboxylate and ethyl 5-amino-3-(4,6-dimethylpyrimidin-2-ylamino)-1-(2-nitrophenylsulfonyl)-1H-pyrazole-4-carboxylate
AUTHOR(S): Wu, Chao; Zhu, You Quan; Li, Hua Bin; Li, Jian Rong; Ren, Xue Ling; Li, Bin; Yang, Hua Zheng
CORPORATE SOURCE: State Key Laboratory, Institute of Elemento-Organic Chemistry, Nankai University, Tianjin, 300071, Peop. Rep. China
SOURCE: Acta Crystallographica, Section C: Crystal Structure Communications (2005), C61(5), o281-o283
CODEN: ACSCEE; ISSN: 0108-2701
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The mol. structures of Et 5-amino-3-(4,6-dimethylpyrimidin-2-ylamino)-1-methyl-1H-pyrazole-4-carboxylate, C13H18N6O2, (I), and Et 5-amino-3-(4,6-dimethylpyrimidin-2-ylamino)-1-(2-nitrophenylsulfonyl)-1H-pyrazole-4-carboxylate, C18H19N7O6S, (II), were determined Crystallog. data are given. There are two intramol. N-H...O bonds and one intermol. N-H...O H bond in (I). The rings formed by the N-H...O H bonds are almost planar. In (II), three intramol. N-H...O H bonds exist.
IT **865648-58-4P 865648-59-5P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and crystal structure of)
RN 865648-58-4 HCAPLUS
CN 1H-Pyrazole-4-carboxylic acid, 5-amino-3-[(4,6-dimethyl-2-pyrimidinyl)amino]-1-methyl-, ethyl ester (9CI) (CA INDEX NAME)



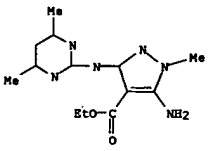
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 865648-59-5 HCAPLUS
CN 1H-Pyrazole-4-carboxylic acid, 5-amino-3-[(4,6-dimethyl-2-pyrimidinyl)amino]-1-[(2-nitrophenyl)sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



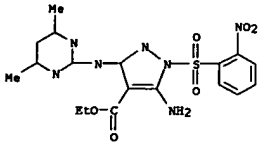
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:354830 HCAPLUS
DOCUMENT NUMBER: 143:386986
TITLE: Synthesis and biological activity of 3-pyrimidylaminopyrazoles
AUTHOR(S): Zou, Xiao-Hao; Wu, Chao; Zhou, Chuan-Zheng; Ren, Xue-Ling; Yang, Hua-Zheng
CORPORATE SOURCE: State Key Laboratory of Elemento-organic Chemistry, Institute of Elemento-Organic Chemistry, Nankai University, Tianjin, 300071, Peop. Rep. China
SOURCE: Gaodeng Xuexiao Huaxue Xuebao (2005), 26(3), 456-460
CODEN: KTHPDM; ISSN: 0251-0790
PUBLISHER: Gaodeng Jiaoyu Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB A series of novel pyrimidylamino-pyrazole derivs. were synthesized and their biol. activities were studied. All of the products were confirmed by 1H NMR and elemental anal., and some of them were characterized by IR and MS. The bioassay results indicated that some of the title compds. have a high fungicidal activity or herbicidal activity. In addition, the structure-activity relationship was discusses.
IT **865648-58-4P 865648-59-5P 866547-69-5P**
866547-70-8P 866547-71-9P 866547-72-0P
866547-74-2P 866547-75-3P 866547-78-6P
866547-79-7P
RL: AGR (Agricultural use); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of pyrimidylaminopyrazoles as fungicide and herbicide)
RN 865648-58-4 HCAPLUS
CN 1H-Pyrazole-4-carboxylic acid, 5-amino-3-[(4,6-dimethyl-2-pyrimidinyl)amino]-1-methyl-, ethyl ester (9CI) (CA INDEX NAME)

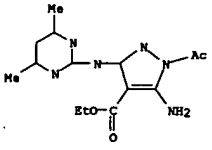


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 865648-59-5 HCAPLUS
CN 1H-Pyrazole-4-carboxylic acid, 5-amino-3-[(4,6-dimethyl-2-pyrimidinyl)amino]-1-[(2-nitrophenyl)sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)

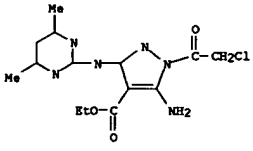
L4 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 866547-69-5 HCAPLUS
CN 1H-Pyrazole-4-carboxylic acid, 1-acetyl-5-amino-3-[(4,6-dimethyl-2-pyrimidinyl)amino]-, ethyl ester (9CI) (CA INDEX NAME)

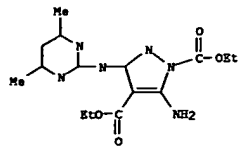


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 866547-70-8 HCAPLUS
CN 1H-Pyrazole-4-carboxylic acid, 5-amino-1-(chloroacetyl)-3-[(4,6-dimethyl-2-pyrimidinyl)amino]-, ethyl ester (9CI) (CA INDEX NAME)

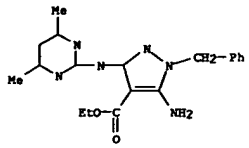


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 866547-71-9 HCAPLUS
CN 1H-Pyrazole-1,4-dicarboxylic acid, 5-amino-3-[(4,6-dimethyl-2-pyrimidinyl)amino]-, diethyl ester (9CI) (CA INDEX NAME)

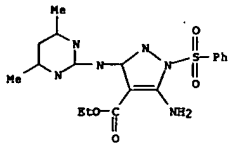
L4 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 866547-72-0 HCAPLUS
CN 1H-Pyrazole-4-carboxylic acid, 5-amino-3-[(4,6-dimethyl-2-pyrimidinyl)amino]-1-(phenylmethyl)-, ethyl ester (9CI) (CA INDEX NAME)

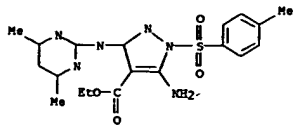


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 866547-74-2 HCAPLUS
CN 1H-Pyrazole-4-carboxylic acid, 5-amino-3-[(4,6-dimethyl-2-pyrimidinyl)amino]-1-(phenylsulfonyl)-, ethyl ester (9CI) (CA INDEX NAME)

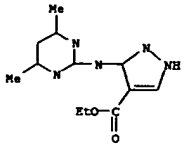


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 866547-75-3 HCAPLUS
CN 1H-Pyrazole-4-carboxylic acid, 5-amino-3-[(4,6-dimethyl-2-pyrimidinyl)amino]-1-[(4-methylphenyl)sulfonyl]-, ethyl ester (9CI) (CA INDEX NAME)

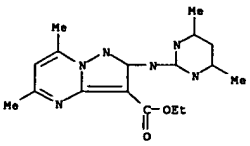
L4 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 866547-78-6 HCAPLUS
CN 1H-Pyrazole-4-carboxylic acid, 3-[(4,6-dimethyl-2-pyrimidinyl)amino]-, ethyl ester (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 866547-79-7 HCAPLUS
CN Pyrazolo[1,5-a]pyrimidine-3-carboxylic acid, 2-[(4,6-dimethyl-2-pyrimidinyl)amino]-5,7-dimethyl-, ethyl ester (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L4 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:300435 HCAPLUS
DOCUMENT NUMBER: 142:373859
TITLE: Preparation of pyrimidine and pyridine derivatives useful as HMG-CoA reductase inhibitors
INVENTOR(S): Ahmad, Saleem; Robl, Jeffrey A.; Ngu, Khehyong
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005030758	A1	20050407	WO 2004-US31212	20040922
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005085497	A1	20050421	US 2004-946055	20040921
PRIORITY APPLN. INFO.:			US 2003-505893P	P 20030925
OTHER SOURCE(S):		MARPAT 142:373859		

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

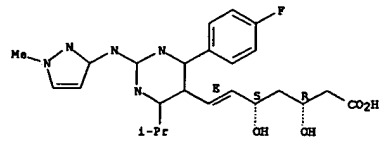
AB Title compds. I [X = N, CR5; R1-2 = H, alkyl, alkoxyalkyl, etc.; R3 = (hetero)aryl, cycloalkyl, etc.; R4 = H, (cyclo)alkyl, haloalkyl, etc.; R5 = H, alkyl; Z = hydroxyalkyl, etc.] are prepared For instance, II is prepared in 5 steps from a substituted pyrimidine, 2-methyl-2H-[1,2,4]triazol-3-ylamine, and a prior art homochiral dihydroxy acetonide derivative I are HMG-CoA reductase inhibitors and are active in inhibiting cholesterol biosynthesis, modulating blood serum lipids, for example, lowering LDL cholesterol and/or increasing HDL cholesterol, and treating hyperlipidemia, dyslipidemia, hormone replacement therapy, hypercholesterolemia, hypertriglyceridemia and atherosclerosis as well as Alzheimer's disease and osteoporosis (no data).

IT 849469-81-4P 849469-83-6P 849470-16-2P 849470-20-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrimidine and pyridine derivs. useful as HMG-CoA reductase inhibitors)

RN 849469-81-4 HCAPLUS
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[(1-methyl-1H-pyrazol-3-yl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, (3R,5S,6E)- (9CI) (CA

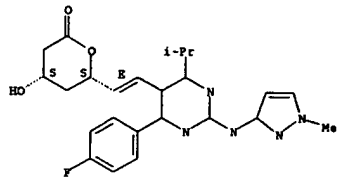
L4 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 849469-83-6 HCAPLUS
CN 2H-Pyran-2-one, 6-[(1E)-2-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[(1-methyl-1H-pyrazol-3-yl)amino]-5-pyrimidinyl]ethenyl]tetrahydro-4-hydroxy-, (4S,6S)- (9CI) (CA INDEX NAME)

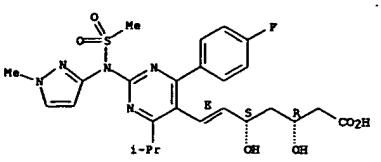
Absolute stereochemistry.
Double bond geometry as shown.



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 849470-16-2 HCAPLUS
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[(1-methyl-1H-pyrazol-3-yl)(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, (3R,5S,6E)- (9CI) (CA INDEX NAME)

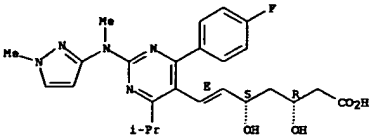
Absolute stereochemistry.
Double bond geometry as shown.

L4 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



RN 849470-20-8 HCAPLUS
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(1-methyl-1H-pyrazol-3-yl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

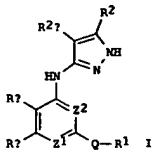


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

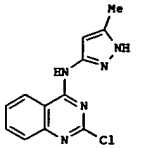
L4 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:140796 HCAPLUS
DOCUMENT NUMBER: 142:240444
TITLE: Preparation of 3-(4-pyrimidinylamino)-1H-pyrazoles as protein kinase inhibitors, especially of Aurora-2 and GSK-3
INVENTOR(S): Bebbington, David; Charrier, Jean-damien; Golec, Julian; Miller, Andrew; Knegtel, Ronald
PATENT ASSIGNEE(S): UK
SOURCE: U.S. Pat. Appl. Publ., 164 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005038023	A1	20050217	US 2003-632428	20030801
PRIORITY APPLN. INFO.:			US 2003-632428	20030801
OTHER SOURCE(S):	MARPAT 142:240444			

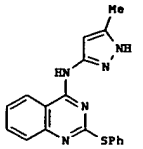
GI



I



II



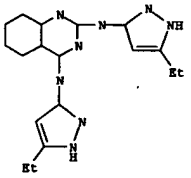
III

AB The title compds. I [Z1 = N, CR8; Z2 = N, CH; and at least one of Z1 and Z2 = N; Rb, Rc = TR3, LZR3; C2RbRc = (un)substituted fused (hetero)cycle; Q = NR4, O, S, etc.; R1 = TD; D = (un)substituted mono- or bicyclic (hetero)aryl, heterocyclyl, carbocyclyl; T = a bond, alkylidene (un)interrupted by O, S, NR4, CO, etc.; Z = alkylidene; L = O, S, SO, SO2,

L4 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)
etc.; R2, R2a = R, TWR6, or C2R2R2a = (un)substituted fused (hetero)cycle; R3 = R, halo, OR, etc.; R = H, (un)substituted aliph., (hetero)aryl, heterocyclyl; R4 = R7, COR7, SO2R7, etc.; W = CO, CO2, CONR6, etc.; R6, R7 = H, alkyl; or N(R6)2 or N(R7)2 = heterocyclyl, heteroaryl] were prepd. For example, the (pyrazolylamino)quinazoline II was refluxed with thiophenol in tert-BuOH to give III. In bioassays, I inhibited the following kinases with Ki values reported < 20 μM: GSK-3β, AURORA-2, CDK-2, ERK2, AKT, and human Src kinase. I are useful for the treatment of diseases assocd. with protein kinases, such as diabetes, cancer, and Alzheimer's disease (no data).

IT **438204-95-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein kinase inhibitor; preparation of (pyrimidinylamino)pyrazoles as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 438204-95-6 HCAPLUS
CN 2,4-Quinazolinediamine, N,N'-bis(5-ethyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L4 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:615605 HCAPLUS
DOCUMENT NUMBER: 137:169539
TITLE: Preparation of 3-(4-pyrimidinylamino)-1H-pyrazoles as protein kinase inhibitors, especially of Aurora-2 and GSK-3, for treatment of cancer, diabetes, and Alzheimer's disease
INVENTOR(S): Bebbington, David; Charrier, Jean-Damien; Golec, Julian M. C.; Miller, Andrew; Knegtel, Ronald
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 335 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002062789	A1	20020815	WO 2001-US51031	20011219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2432222	AA	20020815	CA 2001-2432222	20011219
CA 2432303	AA	20020829	CA 2001-2432303	20011219
WO 2002066461	A1	20020829	WO 2001-US49139	20011219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2432223	AA	20020906	CA 2001-2432223	20011219
WO 2002068415	A1	20020906	WO 2001-US50312	20011219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003004161	A1	20030102	US 2001-26975	20011219
US 6653300	B2	20031125		
US 2003036543	A1	20030220	US 2001-25164	20011219
US 6664247	B2	20031216		
US 2003055068	A1	20030320	US 2001-26967	20011219
US 2003078275	A1	20030424	US 2001-27001	20011219
US 6653301	B2	20031125		
US 2003105090	A1	20030605	US 2001-26966	20011219
EP 1345922	A1	20030924	EP 2001-271061	20011219

L4 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

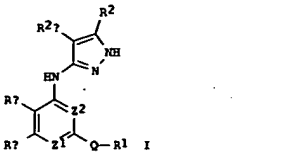
EP 1345927	A1	20030924	EP 2001-994510	20011219	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
EP 1355905	A1	20031029	EP 2001-273861	20011219	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
NZ 526472	A	20040430	NZ 2001-526472	20011219	
JP 2004518703	T2	20040624	JP 2002-563142	20011219	
JP 2004518743	T2	20040624	JP 2002-565976	20011219	
JP 2004519479	T2	20040702	JP 2002-567928	20011219	
US 2004214814	A1	20041028	US 2001-26992	20011219	
CN 1549812	A	20041124	CN 2001-822105	20011219	
NZ 526473	A	20050624	NZ 2001-526473	20011219	
NZ 526471	A	20050826	NZ 2001-526471	20011219	
US 2003004164	A1	20030102	US 2001-34683	20011220	
US 6656939	B2	20031202			
US 2003022885	A1	20030130	US 2001-34019	20011220	
US 6727251	B2	20040427			
ZA 2003004468	A	20040624	ZA 2003-4468	20030609	
ZA 2003004469	A	20040624	ZA 2003-4469	20030609	
ZA 2003004470	A	20040624	ZA 2003-4470	20030609	
ZA 2003004471	A	20040624	ZA 2003-4471	20030609	
ZA 2003004473	A	20040624	ZA 2003-4473	20030609	
ZA 2003004475	A	20040624	ZA 2003-4475	20030609	
ZA 2003004472	A	20040625	ZA 2003-4472	20030609	
ZA 2003004474	A	20040625	ZA 2003-4474	20030609	
NO 2003002704	A	20030821	NO 2003-2704	20030613	
NO 2003002736	A	20030818	NO 2003-2736	20030616	
US 2004224944	A1	20041111	US 2003-624800	20030722	
US 2004116454	A1	20040617	US 2003-692355	20031023	
US 2004157893	A1	20040812	US 2003-722374	20031125	
US 2004132781	A1	20040708	US 2003-736426	20031215	
US 2004167141	A1	20040826	US 2004-775699	20040210	
JP 2005097322	A2	20050414	JP 2004-366925	20041217	

PRIORITY APPLN. INFO.:

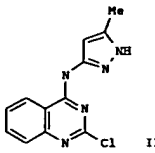
US 2000-257887P	P	20001221
US 2001-286949P	P	20010427
US 2000-232795P	P	20000915
US 2001-952671	A3	20010914
US 2001-955601	A3	20010914
JP 2002-557938	A3	20011219
US 2001-26966	A1	20011219
WO 2001-US49139	W	20011219
WO 2001-US50312	W	20011219
WO 2001-US51031	W	20011219
US 2001-34019	A3	20011220
US 2001-34683	A1	20011220

OTHER SOURCE(S): MARPAT 137:169539

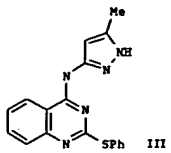
GI



I



II



III

AB 285 Title compds. I [wherein Z1 = N or CR8; Z2 = N or CH; and at least 1 of Z1 and Z2 = N; Rx and Ry = independently TR3 or LZR3; or C2RxRy = (un)substituted fused (hetero)cycle; Q = NR4, O, S, C(R6')2, 1,2-cyclo(prop/but)anediyl, or 1,3-cyclobutanediyl; R1 = TD; D = (un)substituted mono- or bicyclic (hetero)aryl, heterocyclyl, or carbocyclyl; T = a bond or alkylidene chain (un)interrupted by O, S, NR4, CO, CONH, NHCO, SO2, SO2NH, NHSO2, CO2, OCO, OCONH, or NHCO2, with provisos; Z = alkylidene chain; L = O, S, SO, SO2, NR6SO2, SO2NR6, NR6, NR6CO, NR6CO2, NR6CONR6, NR6SO2NR6, NR6NR6, OCONR6, or W; R2 and R2a = independently R, TVR6, or C2R2R2a = (un)substituted fused (hetero)cycle; R3 = R, halo, OR, COR, CO2R, CO(CH2)0-1COR, NO2, CN, SO0-2R, N(R4)2, carbamoyl, sulfamoyl, OCOR, acylamino, hydrazino, ureido, etc.; R = independently H or (un)substituted aliphatic, (hetero)aryl, or heterocyclyl; R4 = independently R7, COR7, carboxy, CON(R7)2, or SO2R7; W = CO, CO2, CONR6, C(R6)2O, C(R6)2SO0-2, C(R6)2SO2NR6, C(R6)2NR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, or C(R6)2NR6CONR6; R6, R6', R7 = independently H or aliphatic; or N(R6)2 or N(R7)2 = independently heterocyclyl or heteroaryl; or C(R6')2 = carbocycle; R8 = R, halo, OR, COR, CO2R, COCOR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2(R4)2, OCOR, NR4COR, NR4CO2(aliphatic), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2] were prepared However, the claims pertain only to 3-(2-amino-4-pyrimidinylamino)-1H-pyrazoles, i.e. Z1 = Z2 = N, and Q = NH. I are protein kinase inhibitors, especially of Aurora-2 and GSK-3. For example, the (pyrazolylamino)quinazoline II was refluxed with thiophenol in t-BuOH to give III. In bioassays, I inhibited the following kinases with Ki values reported < 20 μM: GSK-3β (232 compds.), AURORA-2 (227 compds.), CDK-2 (13 compds.), ERK2 (8 compds.), AKT (10 compds.), and Human Src kinase (183 compds.). I

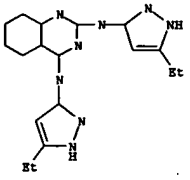
L4 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

are useful for the treatment of diseases assocd. with protein kinases, such as diabetes, cancer, and Alzheimer's disease (no data).

IT **438204-95-6P**, (5-Ethyl-1H-pyrazol-3-yl)[2-(5-ethyl-1H-pyrazol-3-ylamino)quinazolin-4-yl]amine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein kinase inhibitor; preparation of (pyrimidinylamino)pyrazoles as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 438204-95-6 HCAPLUS

CN 2,4-Quinazolinediamine, N,N'-bis(5-ethyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:575069 HCAPLUS

DOCUMENT NUMBER: 137:109292

TITLE: Preparation of 3-(4-pyrimidinylamino)-1H-pyrazoles as protein kinase inhibitors, especially of Aurora-2 and GSK-3, for treatment of cancer, diabetes, and Alzheimer's disease

INVENTOR(S): Bebbington, David; Charrier, Jean-Damien; Davies, Robert; Golec, Julian; Kay, David; Knegtel, Ronald; Patel, Sanjay

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 337 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

PATENT INFORMATION:

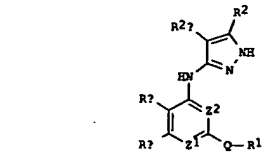
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002059111	A2	20020801	WO 2001-US51120	20011219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2432131	AA	20020801	CA 2001-2432131	20011219
CA 2432303	AA	20020829	CA 2001-2432303	20011219
WO 2002066461	A1	20020829	WO 2001-US49139	20011219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2432223	AA	20020906	CA 2001-2432223	20011219
WO 2002068415	A1	20020906	WO 2001-US50312	20011219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003004161	A1	20030102	US 2001-26975	20011219
US 6653300	B2	20031125		
US 2003036543	A1	20030220	US 2001-25164	20011219
US 6664247	B2	20031216		
US 2003055068	A1	20030320	US 2001-26967	20011219
US 2003078275	A1	20030424	US 2001-27001	20011219
US 6653301	B2	20031125		
US 2003105090	A1	20030605	US 2001-26966	20011219

L4 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

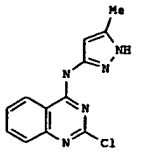
EP 1345922	A1	20030924	EP 2001-271061		20011219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
EP 1345926	A2	20030924	EP 2001-993360		20011219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2001016493	A	20030930	BR 2001-16493		20011219
EP 1355905	A1	20031029	EP 2001-273861		20011219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
NZ 526468	A	20040326	NZ 2001-526468		20011219
NZ 526472	A	20040430	NZ 2001-526472		20011219
JP 2004517926	T2	20040617	JP 2002-559413		20011219
JP 2004518743	T2	20040624	JP 2002-565976		20011219
JP 2004519479	T2	20040702	JP 2002-567928		20011219
US 2004214814	A1	20041028	US 2001-26992		20011219
CN 1549812	A	20041124	CN 2001-822105		20011219
NZ 526473	A	20050624	NZ 2001-526473		20011219
US 2003004164	A1	20030102	US 2001-34683		20011220
US 6656939	B2	20031202			
US 2003022885	A1	20030130	US 2001-34019		20011220
US 6727251	B2	20040427			
ZA 2003004468	A	20040624	ZA 2003-4468		20030609
ZA 2003004469	A	20040624	ZA 2003-4469		20030609
ZA 2003004470	A	20040624	ZA 2003-4470		20030609
ZA 2003004471	A	20040624	ZA 2003-4471		20030609
ZA 2003004473	A	20040624	ZA 2003-4473		20030609
ZA 2003004475	A	20040624	ZA 2003-4475		20030609
ZA 2003004472	A	20040625	ZA 2003-4472		20030609
ZA 2003004474	A	20040625	ZA 2003-4474		20030609
NO 2003002670	A	20030815	NO 2003-2670		20030612
NO 2003002704	A	20030821	NO 2003-2704		20030613
US 2004224944	A1	20041111	US 2003-624800		20030722
US 2004116454	A1	20040617	US 2003-692355		20031023
US 2004157893	A1	20040812	US 2003-722374		20031125
US 2004132781	A1	20040708	US 2003-736426		20031215
US 2004167141	A1	20040826	US 2004-775699		20040210
JP 2005097322	A2	20050414	JP 2004-366925		20041217
PRIORITY APPLN. INFO.:			US 2000-257887P	P	20001221
			US 2001-286949P	P	20010427
			US 2000-232795P	P	20000915
			US 2001-952671	A3	20010914
			US 2001-955601	A3	20010914
			JP 2002-557938	A3	20011219
			US 2001-26966	A1	20011219
			WO 2001-US49139	W	20011219
			WO 2001-US50312	W	20011219
			WO 2001-US51120	W	20011219
			US 2001-34019	A3	20011220
			US 2001-34683	A1	20011220

OTHER SOURCE(S): MARPAT 137:109292
GI

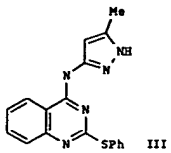
L4 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



I



II



III

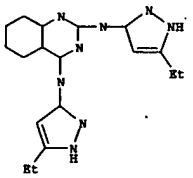
AB Title compds. I [wherein Z1 = N or CR8; Z2 = N or CH; and at least 1 of Z1 and Z2 = N; Rx and Ry = independently TR3 or LZR3; or CZRxRy = (un)substituted fused (hetero)cycle; Q = NR4, O, S, C(6a)2, 1,2-cyclo(prop/but)anediyl, or 1,3-cyclobutanediyl; R1 = TD; D = (un)substituted mono- or bicyclic (hetero)aryl, heterocyclyl, or carbocyclyl; T = a bond or alkylidene chain (un)interrupted by O, S, NR4, CO, CONH, NHCO, SO2, SO2NH, NHSO2, CO2, OCO, OCONH, or NHCO2, with provisos; Z = alkylidene chain; L = O, S, SO, SO2, NR6SO2, SO2NR6, NR6, NR6CO, NR6CO2, NR6CONR6, NR6SO2NR6, NR6NR6, OCONR6, or W; R2 and R2a = independently R, TWR6, or C2R2R2a = (un)substituted fused (hetero)cycle; R3 = R, halo, OR, COR, CO2R, CO(CH2)0-1COR, NO2, CN, SO0-2R, N(R4)2, carbamoyl, sulfamoyl, OCOR, acylamino, hydrazino, ureido, etc.; R = independently H or (un)substituted aliphatic, (hetero)aryl, or heterocyclyl; R4 = independently R7, COR7, carboxy, CON(R7)2, or SO2R7; W = CO, CO2, CONR6, C(R6)2O, C(R6)2SO0-2, C(R6)2SO2NR6, C(R6)2NR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, or C(R6)2NR6CONR6; R6, R6a, R7 = independently H or aliphatic; or N(R6)2 or N(R7)2 = independently heterocyclyl or heteroaryl; or C(R6a)2 = carbocycle; R8 = R, halo, OR, COR, CO2R, COCOR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2(R4)2, OCOR, NR4COR, NR4CO2(aliphatic), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2] were prepared I are protein kinase inhibitors, especially of Aurora-2 and GSK-3. For example, the (pyrazolylamino)quinazoline II was refluxed with thiophenol in t-BuOH to give III. In bioassays, I inhibited the following kinases with Ki values reported < 20 μM: GSK-3β (232 compds.), AURORA-2 (227 compds.), CDK-2 (13 compds.), ERK2 (8 compds.), AKT (10 compds.), and Human Src kinase (183 compds.). I are useful for the treatment of diseases associated with protein kinases, such as diabetes, cancer, and Alzheimer's disease (no data).

L4 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

IT **438204-95-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein kinase inhibitor; preparation of (pyrimidinylamino)pyrazoles as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 438204-95-6 HCAPLUS

CN 2,4-Quinazolinediamine, N,N'-bis(5-ethyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L4 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:555487 HCAPLUS
DOCUMENT NUMBER: 137:125169
TITLE: Preparation of 3-(4-pyrimidinylamino)-1H-pyrazoles as protein kinase inhibitors, especially of Aurora-2 and GSK-3
INVENTOR(S): Bebbington, David; Charrier, Jean-Damien; Golec, Julian; Miller, Andrew; Knegtel, Ronald
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 333 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002057259	A2	20020725	WO 2001-US49401	20011219
WO 2002057259	A3	20030424		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2432129	AA	20020725	CA 2001-2432129	20011219
CA 2432303	AA	20020829	CA 2001-2432303	20011219
WO 2002066461	A1	20020829	WO 2001-US49139	20011219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2432223	AA	20020906	CA 2001-2432223	20011219
WO 2002068415	A1	20020906	WO 2001-US50312	20011219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003004161	A1	20030102	US 2001-26975	20011219
US 6653300	B2	20031125		
US 2003036543	A1	20030220	US 2001-25164	20011219
US 6664247	B2	20031216		
US 2003055068	A1	20030320	US 2001-26967	20011219
US 2003078275	A1	20030424	US 2001-27001	20011219
US 6653301	B2	20031125		
US 2003105090	A1	20030605	US 2001-26966	20011219

L4 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

EP 1345922		A1	20030924	EP 2001-271061	20011219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
EP 1353916		A2	20031022	EP 2001-994323	20011219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
EP 1355905		A1	20031029	EP 2001-273861	20011219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2001016411		A	20031111	BR 2001-16411	20011219
NZ 526472		A	20040430	NZ 2001-526472	20011219
JP 2004517894		T2	20040617	JP 2002-557938	20011219
JP 2004518743		T2	20040624	JP 2002-565976	20011219
JP 2004519479		T2	20040702	JP 2002-567928	20011219
US 2004214814		A1	20041028	US 2001-26992	20011219
CN 1549812		A	20041124	CN 2001-822105	20011219
NZ 526473		A	20050624	NZ 2001-526473	20011219
US 2003004164		A1	20030102	US 2001-34683	20011220
US 6656939		B2	20031202		
US 2003022885		A1	20030130	US 2001-34019	20011220
US 6727251		B2	20040427		
ZA 2003004468		A	20040624	ZA 2003-4468	20030609
ZA 2003004469		A	20040624	ZA 2003-4469	20030609
ZA 2003004470		A	20040624	ZA 2003-4470	20030609
ZA 2003004471		A	20040624	ZA 2003-4471	20030609
ZA 2003004473		A	20040624	ZA 2003-4473	20030609
ZA 2003004475		A	20040624	ZA 2003-4475	20030609
ZA 2003004472		A	20040625	ZA 2003-4472	20030609
ZA 2003004474		A	20040625	ZA 2003-4474	20030609
NO 2003002703		A	20030819	NO 2003-2703	20030613
NO 2003002704		A	20030821	NO 2003-2704	20030613
US 2004224944		A1	20041111	US 2003-624800	20030722
US 2004116454		A1	20040617	US 2003-692355	20031023
US 2004157893		A1	20040812	US 2003-722374	20031125
US 2004132781		A1	20040708	US 2003-736426	20031215
US 2004167141		A1	20040826	US 2004-775699	20040210
JP 2005097322		A2	20050414	JP 2004-366925	20041217

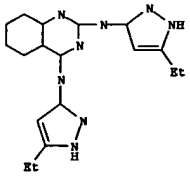
PRIORITY APPLN. INFO.:

US 2000-257887P	P	20001221
US 2001-286949P	P	20010427
US 2000-232795P	P	20000915
US 2001-952671	A3	20010914
US 2001-955601	A3	20010914
JP 2002-557938	A3	20011219
US 2001-26966	A1	20011219
WO 2001-US49139	W	20011219
WO 2001-US49401	W	20011219
WO 2001-US50312	W	20011219
US 2001-34019	A3	20011220
US 2001-34683	A1	20011220

OTHER SOURCE(S): MARPAT 137:125169

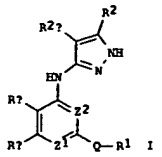
GI

L4 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

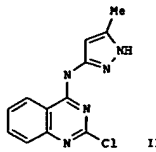


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

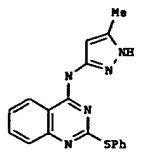
L4 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



I



II



III

AB The title compds. I [Z1 = N, CR8; Z2 = N, CH; and at least one of Z1 and Z2 = N; Rb, Rc = TR3, LZR3; C2RbRc = (un)substituted fused (hetero)cycle; Q = NR4, O, S, etc.; R1 = TD; D = (un)substituted mono- or bicyclic (hetero)aryl, heterocyclyl, carbocyclyl; T = a bond, alkylidene (un)interrupted by O, S, NR4, CO, etc.; Z = alkylidene; L = O, S, SO, SO2, etc.; R2, R2a = R, TWR6, or C2R2R2a = (un)substituted fused (hetero)cycle; R3 = R, halo, OR, etc.; R = H, (un)substituted aliphatic, (hetero)aryl, heterocyclyl; R4 = R7, COR7, SO2R7, etc.; W = CO, CO2, CONR6, etc.; R6, R7 = H, alkyl; or N(R6)2 or N(R7)2 = heterocyclyl, heteroaryl] were prepared For example, the (pyrazolylamino)quinazoline II was refluxed with thiophenol in tert-BuOH to give III. In bioassays, I inhibited the following kinases with Ki values reported < 20 μM: GSK-3β (232 compds.), AURORA-2 (227 compds.), CDK-2 (13 compds.), ERK2 (8 compds.), AKT (10 compds.), and Human Src kinase (183 compds.). I are useful for the treatment of diseases associated with protein kinases, such as diabetes, cancer, and Alzheimer's disease (no data).

IT **438204-95-6P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(protein kinase inhibitor; preparation of (pyrimidinylamino)pyrazoles as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 438204-95-6 HCAPLUS

CN 2,4-Quinazolinediamine, N,N'-bis(5-ethyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)

L4 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:487557 HCAPLUS

DOCUMENT NUMBER: 137:57588

TITLE: Pyrazole compounds useful as protein kinase inhibitors, and therapeutic use thereof

INVENTOR(S): Golec, Julian; Pierard, Francoise; Charrier, Jean-Damien; Bebbington, David

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

PATENT INFORMATION:

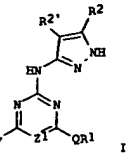
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002050066	A2	20020627	WO 2001-US49585	20011220
WO 2002050066	A3	20030220		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2432303	AA	20020829	CA 2001-2432303	20011219
WO 2002066461	A1	20020829	WO 2001-US49139	20011219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2432223	AA	20020906	CA 2001-2432223	20011219
WO 2002068415	A1	20020906	WO 2001-US50312	20011219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003004161	A1	20030102	US 2001-26975	20011219
US 6653300	B2	20031125		
US 2003036543	A1	20030220	US 2001-25164	20011219
US 6664247	B2	20031216		
US 2003055068	A1	20030320	US 2001-26967	20011219
US 2003078275	A1	20030424	US 2001-27001	20011219
US 6653301	B2	20031125		
US 2003105090	A1	20030605	US 2001-26966	20011219
EP 1345922	A1	20030924	EP 2001-271061	20011219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

L4 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

EP 1355905		A1	20031029	EP 2001-273861	20011219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
NZ 526472		A	20040430	NZ 2001-526472	20011219
JP 2004518743		T2	20040624	JP 2002-565976	20011219
JP 2004519479		T2	20040702	JP 2002-567928	20011219
US 2004214814		A1	20041028	US 2001-26992	20011219
CN 1549812		A	20041124	CN 2001-822105	20011219
NZ 526473		A	20050624	NZ 2001-526473	20011219
CA 2432872		AA	20020627	CA 2001-2432872	20011220
AU 2002031166		A5	20020701	AU 2002-31166	20011220
US 2003004164		A1	20030102	US 2001-34683	20011220
US 6656939		B2	20031202		
US 2003022885		A1	20030130	US 2001-34019	20011220
US 6727251		B2	20040427		
EP 1345928		A2	20030924	EP 2001-991439	20011220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004516292		T2	20040603	JP 2002-551562	20011220
NZ 526474		A	20051028	NZ 2001-526474	20011220
ZA 2003004468		A	20040624	ZA 2003-4468	20030609
ZA 2003004469		A	20040624	ZA 2003-4469	20030609
ZA 2003004470		A	20040624	ZA 2003-4470	20030609
ZA 2003004471		A	20040624	ZA 2003-4471	20030609
ZA 2003004473		A	20040624	ZA 2003-4473	20030609
ZA 2003004475		A	20040624	ZA 2003-4475	20030609
ZA 2003004472		A	20040625	ZA 2003-4472	20030609
ZA 2003004474		A	20040625	ZA 2003-4474	20030609
NO 2003002704		A	20030821	NO 2003-2704	20030613
US 2004224944		A1	20041111	US 2003-624800	20030722
US 2004116454		A1	20040617	US 2003-692355	20031023
US 2004157893		A1	20040812	US 2003-722374	20031125
US 2004132781		A1	20040708	US 2003-736426	20031215
US 2004167141		A1	20040826	US 2004-775699	20040210
JP 2005097322		A2	20050414	JP 2004-366925	20041217
PRIORITY APPLN. INFO.:				US 2000-257887P	P 20001221
				US 2001-286949P	P 20010427
				US 2000-232795P	P 20000915
				US 2001-952671	A3 20010914
				US 2001-955601	A3 20010914
				JP 2002-557938	A3 20011219
				US 2001-26966	A1 20011219
				WO 2001-US49139	W 20011219
				WO 2001-US50312	W 20011219
				US 2001-34019	A3 20011220
				US 2001-34683	A1 20011220
				WO 2001-US49585	W 20011220

OTHER SOURCE(S): MARPAT 137:57588
GI

L4 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

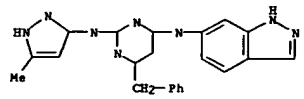


I

AB The invention describes pyrazole compds. I [Z1 = N, CR8; Q = O, S, etc.; R1 = T-Ring D; T = valence bond, alkylidene chain; Ring D = 5-7-membered monocyclic ring, 8-10-membered bicyclic ring; R2, R2' = H, (un)substituted C1-6 aliphatic, (un)substituted C6-10 aryl, etc.; Ry = (un)substituted C1-6 aliphatic, (un)substituted C6-10 aryl, etc.; R8 = halo, NO2, CN, etc.]. The compds. are useful as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease.

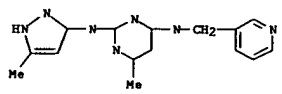
IT **439076-30-9 439076-31-0 439076-36-5**
439076-37-6 439076-38-7 439076-39-8
439076-40-1 439076-41-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pyrazole compds. as protein kinase inhibitors, and therapeutic use)

RN 439076-30-9 HCAPLUS
CN 2,4-Pyrimidinediamine, N4-1H-indazol-6-yl-N2-(5-methyl-1H-pyrazol-3-yl)-6-(phenylmethyl)- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

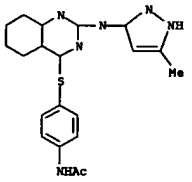
RN 439076-31-0 HCAPLUS
CN 2,4-Pyrimidinediamine, 6-methyl-N2-(5-methyl-1H-pyrazol-3-yl)-N4-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

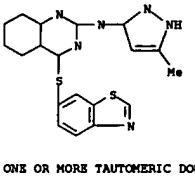
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 439076-36-5 HCAPLUS
CN Acetamide, N-[4-[[2-[(5-methyl-1H-pyrazol-3-yl)amino]-4-quinazolinyl]thio]phenyl]- (9CI) (CA INDEX NAME)



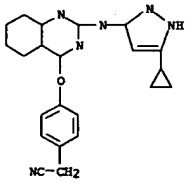
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 439076-37-6 HCAPLUS
CN 2-Quinazolinamine, 4-(6-benzothiazolylthio)-N-(5-methyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

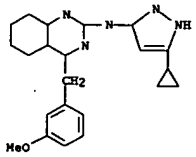
RN 439076-38-7 HCAPLUS
CN Benzeneacetonitrile, 4-[[2-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]-4-quinazolinyl]oxy]- (9CI) (CA INDEX NAME)



L4 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

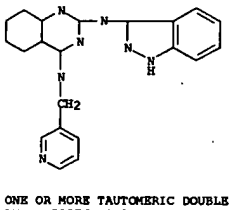
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 439076-39-8 HCAPLUS
CN 2-Quinazolinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-4-[(3-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



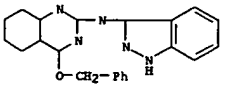
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 439076-40-1 HCAPLUS
CN 2,4-Quinazolinediamine, N2-1H-indazol-3-yl-N4-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 439076-41-2 HCAPLUS
CN 2-Quinazolinamine, N-1H-indazol-3-yl-4-(phenylmethoxy)- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L4 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:487556 HCAPLUS
DOCUMENT NUMBER: 137:47221
TITLE: Preparation of 3-(4-pyrimidinylamino)-1H-pyrazoles as protein kinase inhibitors, especially of Aurora-2 and GSK-3, for treatment of cancer, diabetes, and Alzheimer's disease
INVENTOR(S): Bebbington, David; Charrier, Jean-Damien; Davies, Robert; Everitt, Simon; Kay, David; Knegtel, Ronald; Patel, Sanjay
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 342 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002050065	A2	20020627	WO 2001-US49140	20011219
WO 2002050065	A3	20021024		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2432799	AA	20020627	CA 2001-2432799	20011219
AU 2002034047	A5	20020701	AU 2002-34047	20011219
CA 2432303	AA	20020829	CA 2001-2432303	20011219
WO 2002066461	A1	20020829	WO 2001-US49139	20011219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2432223	AA	20020906	CA 2001-2432223	20011219
WO 2002068415	A1	20020906	WO 2001-US50312	20011219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003004161	A1	20030102	US 2001-26975	20011219
US 6653300	B2	20031125		

L4 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

US 2003036543	A1	20030220	US 2001-25164	20011219
US 6664247	B2	20031216		
US 2003055068	A1	20030320	US 2001-26967	20011219
US 2003078275	A1	20030424	US 2001-27001	20011219
US 6653301	B2	20031125		
US 2003105090	A1	20030605	US 2001-26966	20011219
EP 1345922	A1	20030924	EP 2001-271061	20011219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EP 1345925	A2	20030924	EP 2001-985059	20011219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EP 1355905	A1	20031029	EP 2001-273861	20011219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NZ 526472	A	20040430	NZ 2001-526472	20011219
JP 2004516291	T2	20040603	JP 2002-551561	20011219
JP 2004518743	T2	20040624	JP 2002-565976	20011219
JP 2004519479	T2	20040702	JP 2002-567928	20011219
US 2004214814	A1	20041028	US 2001-26992	20011219
CN 1549812	A	20041124	CN 2001-822105	20011219
NZ 526473	A	20050624	NZ 2001-526473	20011219
NZ 526469	A	20051028	NZ 2001-526469	20011219
US 2003004164	A1	20030102	US 2001-34683	20011220
US 6656939	B2	20031202		
US 2003022885	A1	20030130	US 2001-34019	20011220
US 6727251	B2	20040427		
ZA 2003004468	A	20040624	ZA 2003-4468	20030609
ZA 2003004469	A	20040624	ZA 2003-4469	20030609
ZA 2003004470	A	20040624	ZA 2003-4470	20030609
ZA 2003004471	A	20040624	ZA 2003-4471	20030609
ZA 2003004473	A	20040624	ZA 2003-4473	20030609
ZA 2003004475	A	20040624	ZA 2003-4475	20030609
ZA 2003004472	A	20040625	ZA 2003-4472	20030609
ZA 2003004474	A	20040625	ZA 2003-4474	20030609
NO 2003002671	A	20030818	NO 2003-2671	20030612
NO 2003002704	A	20030821	NO 2003-2704	20030613
US 2004224944	A1	20041111	US 2003-624800	20030722
US 2004116454	A1	20040617	US 2003-692355	20031023
US 2004157893	A1	20040812	US 2003-722374	20031125
US 2004132781	A1	20040708	US 2003-736426	20031215
US 2004167141	A1	20040826	US 2004-775699	20040210
JP 2005097322	A2	20050414	JP 2004-366925	20041217

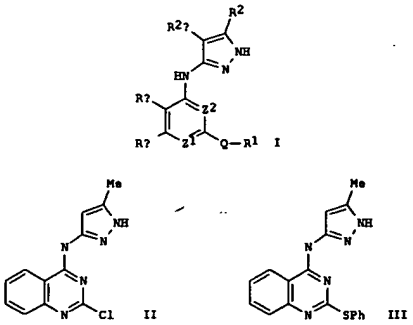
PRIORITY APPLN. INFO.:

US 2000-257887P	P	20001221
US 2001-286949P	P	20010427
US 2000-232795P	P	20000915
US 2001-952671	A3	20010914
US 2001-955601	A3	20010914
JP 2002-557938	A3	20011219
US 2001-26966	A1	20011219
WO 2001-US49139	W	20011219
WO 2001-US49140	W	20011219
WO 2001-US50312	W	20011219
US 2001-34019	A3	20011220
US 2001-34683	A1	20011220

OTHER SOURCE(S): MARPAT 137:47221

L4 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

GI



I

II

III

AB Title compds. I [wherein Z1 = N or CR8; Z2 = N or CH; and at least 1 of Z1 and Z2 = N; Rx and Ry = independently TR3 or LZR3; or C2RxRy = (un)substituted fused (hetero)cycle; Q = NR4, O, S, C(6a)2, 1,2-cyclo(prop/but)anediyl, or 1,3-cyclobutanediyl; R1 = TD; D = (un)substituted mono- or bicyclic (hetero)aryl, heterocyclyl, or carbocyclyl; T = a bond or alkylidene chain (un)interrupted by O, S, NR4, CO, CONR, NRCO, SO2, SO2NR, NRSO2, CO2, OCO, OCONR, or NRCO2, with provisos; Z = alkylidene chain; L = O, S, SO, SO2, NR6SO2, SO2NR6, NR6, NR6CO, NR6CO2, NR6CONR6, NR6SO2NR6, NR6NR6, OCONR6, or W; R2 and R2a = independently R, TWR6, or C2R2R2a = (un)substituted fused (hetero)cycle; R3 = R, halo, OR, COR, CO2R, CO(CH2)0-1COR, NO2, CN, SO0-2R, N(R4)2, carbamoyl, sulfamoyl, OCOR, acylamino, hydrazino, ureido, etc.; R = independently H or (un)substituted aliphatic, (hetero)aryl, or heterocyclyl; R4 = independently R7, COR7, carboxy, CON(R7)2, or SO2R7; W = CO, CO2, CONR6, C(R6)2O, C(R6)2SO0-2, C(R6)2SO2NR6, C(R6)2NR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, or C(R6)2NR6CONR6; R6, R6a, R7 = independently H or aliphatic; or N(R6)2 or N(R7)2 = independently heterocyclyl or heteroaryl; or C(R6a)2 = carbocycle; R8 = R, halo, OR, COR, CO2R, COCOR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2(R4)2, OCOR, NR4COR, NR4CO2(aliphatic), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2] were prepared I are protein kinase inhibitors, especially of Aurora-2 and GSK-3. For example, the (pyrazolylamino)quinazoline II was refluxed with thiophenol in t-BuOH to give III. In bioassays, I inhibited the following kinases with Ki values reported < 20 μM: GSK-3β (232 compds.), AURORA-2 (227 compds.), CDK-2 (13 compds.), ERK2 (8 compds.), AKT (10 compds.), and Human Src kinase (183 compds.). I are useful for the treatment of diseases associated with protein kinases, such as diabetes, cancer, and Alzheimer's disease

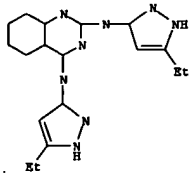
L4 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)

(no data).

IT 438204-95-6P, (5-Ethyl-1H-pyrazol-3-yl)[2-(5-ethyl-1H-pyrazol-3-ylamino)quinazolin-4-yl]amine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein kinase inhibitor; preparation of (pyrimidinylamino)pyrazoles as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 438204-95-6 HCAPLUS

CN 2,4-Quinazolinediamine, N,N'-bis(5-ethyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE